

U.S. Application No. 09/864,637  
Attorney Docket No. 00801.0197.NPUS00

**REMARKS**

Claims 15-31 and 43-45 are pending. Claims 47-51 have been added. Claims 1-14, 32-42 and 46 have been canceled without prejudice.

Claims 1-8, 10-32 and 37-46 were rejected under 35 USC 112, second paragraph as being indefinite in several recitations. Since several of these claims have been canceled without prejudice, those matters are moot and need no further discussion.

As for the examiner's assertions that claim 15 is indefinite in the recitation "library is represented in "lower amounts" or "higher amounts" as being relative and indefinite, this rejection is respectfully traversed. While one might consider the term relative, the specification example shows about 30% of the total as low abundance as recited in the specification on page 29, lines 9-11 and newly added claim 47. A description of what constitutes "lower amounts" is provided in the description of Figure 3 and exemplified therein. A more general definition and various examples may be found on page 19, lines 5 to the middle of page 21. It should be appreciated that the exact numbers will depend on the specific cell/tissue/organism sample one is using. Regardless, the same general method as claimed applies.

Because the specification technically refers to "low" and "high" when referring to abundance rather than lower and higher, the claims have been amended to reflect this difference in wording but not meaning. Claim 15 has been amended to recite different language, which clearly distinguishes one group from another group avoiding any possible interpretation of

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indefiniteness. Claims 43 and 44 were rejected for essentially the same reason and each has been amended accordingly.

As for claim 30 being indefinite as to the term "said group of members", it is clear from line 1 of claim 30 that everything refers to "said identifying of step (e)". Thus the "said group of members" of claim 30 refers to the same "said group of members" found in step (e) of claim 15. Accordingly, this rejection should be withdrawn.

Claims 1-5, 7 and 10-14 were rejected under 35 USC 103(a) as unpatentable over Nelson et al. in view of Frohman et al. These claims have been canceled without prejudice and thus the rejection is moot.

Claim 6 was rejected under 35 USC 103 as being unpatentable over Nelson et al. in view of Frohman et al. as applied above in further view of Somerville. This claim has been canceled without prejudice and thus the rejection is moot.

Claim 8 was rejected under 35 USC 103 as being unpatentable over Nelson et al. in view of Frohman et al. as applied above in further view of El-Meanawy et al. This claim has been canceled without prejudice and thus the rejection is moot.

Claim 38 was rejected under 35 USC 103 as being unpatentable over Nelson et al. in view of Frohman et al. in further view of Gress et al. This claim has been canceled without prejudice and thus the rejection is moot.

Claims 39, 40 and 41 were rejected under 35 USC 103 as being unpatentable over Nelson et al. in view of Frohman et al. in further view of Xu et al. These claims have been canceled without prejudice and thus the rejection is moot.

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Claims 15-19, 21, 23-31 and 43-46 were rejected under 35 USC 103 as being unpatentable over Nelson et al. in view of Carninci et al. These claims should not be confused with claims 1+, which have been canceled. Claims 15+ are depicted by all of specification Figure 3 including the sub-protocol shown in specification Figure 3 on the left side in thin lines. Claims 1+ are shown by the thicker lines on the right side of specification Figure 3. The sub-protocol is not disclosed or rendered obvious by any combination of references cited. Steps d, e and f in particular are not suggested by prior art. Other differences between the present invention and the references also exist.

Nelson et al. describes a normalization procedure by using labeled cDNA to apply a negative selection to detect high abundance library clones. This procedure has some similarities to that shown as thick black lines in Figure 3. Carninci et al. discloses a similar procedure and combines it with a "subtraction" procedure using drivers from a minilibrary. This "subtraction" procedure is somewhat similar to that in Gress et al. and Xu et al.

However, all of these "subtractions" use drivers that are cDNA from different sample sources, such as different tissues, different species, etc. The goal is to obtain genes specific to that original sample source such as cancer specific genes instead of genes expressed in different or normal tissues. The drivers used are NOT from a subgroup of the high abundance clones of the cDNA library being normalized as is claimed. Thus, the steps d, e and f are not taught or suggested by any combination of the references.

The goal of the present invention is normalization, not subtraction. Indeed, the present invention creates a library from many different tissues (see claims 48-51). The present invention seeks to be comprehensive and normalized, not "subtract" any cDNA which seem uninteresting.

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Neither reference separates the group of high abundance sample cDNAs into subgroups that are then used to hybridize to each other. Even less is the use of each subgroup repeatedly to hybridize with other subgroups (see claim 43 in particular). Therefore, the steps claimed in claims 15+ are not taught nor suggested by these references. Accordingly, the rejection should be withdrawn.

Claim 20 was rejected under 35 USC 103 as being unpatentable over Nelson et al. in view of Carninci et al. and further in view of Somerville et al. The reasons why the basic rejection is overcome are given above. Somerville et al. adds nothing as to the normalization and handling of subgroups of cDNAs. Therefore, this dependant claim should stand with its independent claim and the rejection withdrawn.

Claim 22 was rejected under 35 USC 103 as being unpatentable over Nelson et al. in view of Carninci et al. and further in view of El-Meanawy et al. The reasons why the basic rejection is overcome are given above. El-Meanawy et al. adds nothing as to the normalization and handling of subgroups of cDNAs. Therefore, this dependant claim should stand with its independent claim and the rejection withdrawn.

### CONCLUSIONS

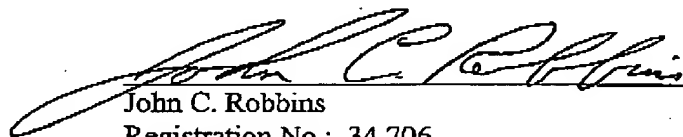
In view of the amendments and comments above, the rejections have been overcome. Reconsideration, withdrawal of the rejections and early indication of allowance are respectfully requested.

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The commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No. 500933.

Respectfully submitted,

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